

**AUTHENTICATION OF PROMOTIONAL MATERIALS OF
MEDICINAL DRUGS IN NEPAL: AN EVIDENCE BASED APPROACH**

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Article Received on
05 October 2023,

Revised on 25 October 2023,
Accepted on 15 Nov. 2023

DOI: 10.20959/wjpr202321-30344



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ABSTRACT

In Nepal, the physician depends on the information provided by marketing representatives. The information containing in promotional material is not in accordance to the requirement of the National regulation authority. The information in the promotional materials is often misleading. The promotional materials are analyzed critically and audited with the help of currently available evidences in the medical literatures and the questionnaire was built to obtain the information about the marketing representatives. 1125 promotional materials were collected from the marketing office of the pharmaceutical companies, hospitals (Bir Hospital, Tribhuvan University Teaching Hospital, Nidan Hospital Pvt Ltd, Sumeru City Hospital) and marketing representatives in Kathmandu valley. The collected materials were analyzed for the misleading claims in those materials which are not substantiated by the scientific evidences. Out of total collected materials 780 were of Nepalese manufacturing company whole 345 where of multinational company. The collected promotional material have the active ingredients (99.37%), brand name (100%), source citation (12.98%), and the excipients and their role in 5 out of 1125 (0.44%) in the promotional material. Similarly only 4.44% of promotional material had information about date of production of information. Also,

information about indication was present in 97.60%, side effect and major ADR's in 42.67 % and precaution, contraindication and warnings in 37.33% of total collected promotional material. The misleading claims are overstated (71.36%), ambiguous (7.72%), false (4.56%) and debatable (16.36%) were identified by examining the promotional material critically. The information in promotional claims must be accurate, scientifically sound, truthful, objective and balanced and must reflect the correct state of knowledge. And the medical representatives should have appropriate scientific training and product knowledge.

KEYWORDS: *Promotional material. Misleading claims, Pharmaceutical marketing.*

INTRODUCTION

Background: Practicing medicine is an art as well as science. The physician is expected to prescribe drugs to the patients and the medicines are expected to give a reasonable cure. Practitioners are guided by their own clinical knowledge acquired during the formal medical training, experience and periodic refurbishment of knowledge obtained by attending the continuing medical education programs.^[1] Drug promotion is any activity which involves advertising, detailing, freebies, and sponsoring of conferences and symposia by a drug company which is intended to increase the sales of its products.^[2] The main purpose of drug promotion is to persuade people to buy more drugs and/or to pay higher prices.^[3] Heavy promotion of new drugs lead to widespread prescribing and use before the safety profile of these products is fully understood. Newer more expensive medicines displace older, less costly ones without any evidence of an improvement in therapeutic outcomes.^[4]

The pharmaceutical promotion and marketing expenditure average 20-30% of sales turnover or about two to three times the average expenditure on research and development.^[5] The medical practitioner has the freedom to decide the drugs required for their patient for any given ailment. The Doctors in private practice, or who are graduated long ago report the highest use of promotion as a source of drug information. Promotion influences attitudes more than doctors realize.^[4] In country like Nepal, marketing representatives are the major source of information.^[6] The information on guide to good prescribing^[7] had shown that over 90% of doctors see medical representatives (MRs) and depend heavily on them as a source of information about medicines and therapeutics.^[7] Many doctors cite marketing representatives as one of the main sources of information on the use of new drugs.^[8] The information provided by medical representatives brings attitudes in the sale of the drug.^[9]

The printed promotional materials used by the medical representatives, banners and posters at conferences and exhibition stalls and direct mailing to doctors usually include rational-product.^[10] The printed promotional materials help the physician to provide the information about the drug molecule and promote the rational prescription.

In Nepal various guidelines are being only written and the implementation is lacking. The National regulatory authority, Department of drug Administration with Graduate Pharmacy Association of Nepal (GPAN) has formulated the ethical promotional guideline on the promotion material.^[11] The required information is lacking in many promotional materials.^[12] The essentiality of the desired information in the promotion materials is important in identifying whether the pharmaceutical company is strongly implementing the requirements of the guidelines.

The study on the promotional materials to analyze for the availability for the information, misleading claims may help the policy maker in the formulation and implementation of rules and regulation regarding the promotional material's content and its use.

The research is conducted in order to fulfill the following objectives.

- i. To analyze critically and audit the promotional materials of the medicinal drugs with the help of currently available evidences in the medical literature and national guidelines.
- ii. To examine whether the collected promotional material is following the guideline provided by WHO and DDA on promotion on material.
- iii. To identify and analyze the promotional misleading claims based on the evidence.

MATERIALS AND METHODOLOGY

Different promotional materials like flash card leave behind card, magazines, general information brochures, leaflets, literatures, drugs status of different companies, and any other available printed materials were collected from the hospital and marketing representatives.

Method of material collection: The materials were collected by different methods

- From marketing and distribution branches of the pharmaceutical company available in the valley.
- Marketing representatives

- Doctors cabin i.e. those promotional materials left for the doctors by the marketing representatives from Bir Hospital and TUTH (Tribhuvan University Teaching Hospital), Patan Hospital. Nidan Hospital Pvt.Ltd, Sumerucity Hospital Pvt.Ltd.)
- Pharmacy counter

Inclusion/ Exclusion criteria: All forms of printed promotional materials were included except

- Detailed literature
- Drug status of different companies
- Reminder card and Training material

Sample size: The total of 1125 promotional materials were collected and evaluated.

Method of evaluation of promotional material

1. Availability of information according to WHO guideline and DDA guideline

The collected material was then analyzed to find out whether they fulfill the criteria as per national guideline. The requirements of the criteria given by WHO guidelines and DDA guidelines on ethical promotion of material^[15,19] were used for analysis. The collected materials were analyzed for:

a. Presence /absence of general information in promotional material

- i. Name of active ingredients
- ii. Brand name

b. Presence/ absence of information regarding clinical use of the medicine

- i. Approved therapeutic use
- ii. Side effect and major ADRs
- iii. Precautions, contra-indications and warnings
- iv. Major interactions

c. Presence/ absence dose related information

- i. Content of active ingredient(s) per dosage form or regimen
- ii. Name of all the excipients and their role in the dosage form
- iii. Dosage form and/ or regimen
- iv. Presence/ absence of other necessary information

d. Presence/ absence of other necessary information

- i. Date of production of information
- ii. Name and address of manufacturer, and distributor

iii. Reference to scientific literature

2. Analysis on promotional claims made in promotional materials

The claims in the promotional material were analyzed in order to find out validate the degree of correctness. Misleading claims were identified, and the identified claims were further divided as:

1. **Debatable claims:** when the claims in the question is controversial in nature or not settled by the scientifically and lack of evidence. The validity of the claims will also be included and the claims which are yet to be proven is included in this claim.
2. **Ambiguous claim:** when the claim is found to be unclear in the promotional material.
3. **Overstated claims:** when insignificant merit of the drugs is found to be magnified intentionally and unnecessarily and make it a significant one.
4. **False claims:** when the claims in the question was found to be beyond the truth. This classification is based on the research conducted on the promotional material in Pakistan^[13] and in Bangladesh.^[14]

RESULT AND DISCUSSION

Study on the promotional materials and their evaluation was carried out through various methods.

The collected promotional material was classified on the basis of drug being manufactured in Nepal and abroad and presented in the figure below.

Table 1: Classification on the basis of manufacturer.

S. N.	Manufactures	Total number of promotional material (out of 1125)
1	Nepalese company	780
2	Foreign company	345

1. Availability of information on the promotion material according to WHO guideline and DDA guideline

The general information in the promotional material is presented in the Table 2. The analysis of the information related to the clinical use of medicine is presented in Table 3. Table 4 shows number of the promotional material having of dose related information. The promotional materials having other criteria are presented in Table 5.

1.1 Number of promotional material having general information

Table 2: Promotional material having general information.

S. N.	Promotional Material having following information	Number of promotional material (Out of Total 1125)	Percentage
1	Name of Active ingredients	1025	91.11%
2	Brand Name	1125	100.00%

In our study, the general information like name of the active ingredients was present in the majority of promotional materials i.e. 1025 out of 1125(91.11%). This is almost similar to evaluation of promotional materials in the hospital setting carried out in Manipal, Pokhara, Nepal^[15] where 87.87% of the promotional materials have the name of the active ingredients and nearly about 80% of promotional materials in Indonesia contain the name of active ingredient.^[16,17]

Similarly, brand name was include in 100% of the promotional material which is similar to the results Obtained from the studies carried out in Manipal in which each and every promotional materials got the Brand name, also same result was found in Indonesia.^[16] This indicated that the drug is promoted through the brand details rather than a generic. The Advertising drugs by their generic names, rather than brand names, gives flexibility to drug prescription and may be economical to patient.^[18]

1.2 Number of promotional material having information related to clinical use

Table 3: Promotional material having information related to clinical use.

S. N.	Promotional Material having following information	Number of promotional material (Out of Total 1125)	Percentage
1	Indication (approved therapeutic use)	1098	97.60%
2	Side effect and Major ADR's	480	42.67%
3	Precautions, contraindication and warnings	420	37.33%
4	Major drug interaction	302	26.84 %

In our study, relating to the analysis of the promotional materials having information related to clinical use, 1098 (97.60%)promotional materials had information related to therapeutic uses, side effects 480(42.67%) similar to that of the study carried in Manipal where indication and side effects where outlined in 87.88% and 33.33% of promotional materials respectively.

So we can confirm that the promotional material are more focused on the therapeutic use and indication though precautions, contraindications, adverse drug interactions, warning are also to be mentioned as per the guidelines. Absence of this information could lead to increased cases of irrational use of drugs, patient vulnerable to side effects and toxicities.

1.3 Number of promotional material having dose related information

Table 4: Promotional material having dose related information.

S. N.	Promotional material having following information	Number of promotional material (Out of Total 1125)	Percentage
1	Content of active ingredient(s) per dosage form or regimen	1056	93.87%
2	Others ingredients information	5	0.44%
3	Dosage form or regiment	1119	99.47%

Further, in our study we found content of active ingredients per dosage were mentioned in 1056 (93.87%) and dosage form or regimen were found in about 1119 (99.47%) of the promotional materials. Information related to excipients and other ingredients were found in 5 promotional material. It is very important to mention about the name and roles of the ingredients as many of the ingredients may show different reactions in different individual. For example, iatrogenic mercury deposits takes place in the crystalline lens resulting from the eye drops containing phenyl mercuric nitrate 0.004% used for longer period of time leading to yellow brown discoloration of lens capsule. Thus the indication of presence of phenyl mercuric nitrate is essential in eyes drops if they are to be indicated for the long term use.^[19]

1.4 Number of promotional material having other criteria

Table 5: Promotion material having other criteria.

S. N.	Promotional Material having following information	Number of promotional material (Out of Total 1125)	Percentage
1	Date of production of information	50	4.44%
2	Name and address of manufacturer and/or distributor	998	88.71%
3	Reference to scientific literature	146	12.98%

The date of preparation and name of the manufacture are important parameter as the information are being reviewed and new findings related to indication, contraindication, banning of the drugs are being repeatedly updated. The information on date of printing

(month/ year) together with a code number must be indicated. This will help in establishing control lists of promotional/ product information material.

12.98% of the promotional material contained the references indicating from where the information related to particular drugs was collected. This finding is less than that carried in a South American country Argentina where about 60% of 30 promotional materials had statements supported by the cited reference.^[20]

Similarly in our study none of the promotional materials had all the necessary information required as per DDA and WHO Ethical criteria for Medicinal Drug promotion. We found that there were difficulty in accessing the references mentioned in the promotional materials and information regarding efficacy, safety etc were not always supported by the scientific facts and studies.

Effective drug regulation could be a sensible solution to the problem related to the unethical drug promotion in Nepal where the promotional materials could largely influence the prescription behavior of the clinicians.

2. Misleading claims in promotional material

All the promotion material was identified and analyzed for overstated, ambiguous, false and controversial claims using different available journals, literatures, monographs and internet sources.

The claims made by pharmaceutical company are often misleading.^[12] The claims which are misleading are 220 (19.56%) in number. Out of total misleading claims 16.36% were debatable claims, supported by scientific evidences. The overstated claims accounts for 71.36% of the entire unjustifiable promotional claims. The ambiguous and false claims are 7.72% and 4.56% respectively. The previous studies carried out on the claims made in promotional material in Pakistan^[13] and in Bangladesh^[14] show that the misleading claims were 32% and 22% respectively. There is more exaggeration of claims on the promotional material. Information in the promotional materials is often presented with magnified benefits having little importance in practice.

2.1 Overstated claim

Many pharmaceutical companies (National and International) were found to have overstated certain facts about their products. More than half of the misleading information found was

detected overstated i.e. 157 out of 220 (71.36%). A promotional material of azithromycin makes the claim that it does not have any significant drug interactions but the drugs like cyclosporine and digoxin increases the level of azithromycin.^[21] The lists of such claims were identified.

2.2 Ambiguous claim

We found that the promotional claims made by the pharmaceutical company are unclear and even vague. Of the total misleading claims in promotional material there are 17 claims, which are ambiguous or having no clear information regarding the claim made by the manufacturer. A promotional material of anesthetic drugs midazolam has the claim that there is less inter individual variation and rapid recovery of the drug but it has been cited that the patients with the renal impairment may have longer elimination half life for midazolam and its metabolites which may result in the slower recovery of the drug.^[22]

2.3 False claim

Some of the claims made by the pharmaceutical company are beyond the truth. The least of the misleading information's where completely false i.e. only 4.56%. In the promotional material where Levofloxacin may result a cardiac arrhythmia due to prolongation of QT interval, but one of the manufactures claim it to have no cardio toxicities.^[16,22]

2.4 Debatable claim

The promotional debatable claim made by the pharmaceutical company was found to be 36 out of 220. One of the promotional material has claimed that Cefuroxime axetil's absorption and bioavailability is not affected by food but one of the information claim that bioavailability is increased by 20% when taken with food than empty stomach.^[23]

Table 6: Misleading claims in promotional material.

<i>S. N.</i>	<i>Misleading claims</i>	<i>Number (out of total 220)</i>	<i>Percentage</i>
1	Overstated Claim	157	71.36%
2	Ambiguous Claim	17	7.72%
3	False Claim	10	4.56 %
4	Debatable Claim	36	16.36%

List of examples of misleading claims

Table 7: List of examples of misleading claims.

S. N.	Misleading Claims	Drugs	Claims	Anticlaims
1	Overstated	Aceclofenc	excellent efficacy in acute and chronic inflammation pain.	it is as effective as other NSAIDs in patient with osteoarthritis, RA ^[25]
2		Antacid preparation	highly potent antacid.	no convincing evidence of its validity, only logical support for this claim ^[26]
3		Azithromycin	more potent than other macrolides against gram negative pathogens.	other macrolides have similar antibacterial spectrum invitro ^[27]
4		Cefixime	effective against any type of infection	not effective against viral infection ^[28]
5		Diclofenac	superior, safe and patient friendly NSAIDs	compared to diclofenac, nimusulide is significantly better than diclofenac in relieving pain. Besides, diclofenac is contraindicated to third-trimester pregnancy, active peptic ulceration or GI bleeding, severe renal and liver insufficiency. ^[29]
6		Losartan	for better and effective control of HTN safely	losartan may reduce kidney function in some patients and should not be used by patients who have ilateral renal artery stenosis narrowing of both arteries going to the kidneys. ^[30]
7	Ambiguous	Mecobalamine	should be considered in all neurological disease	not all the disorder is treated with ecobalamine except neuralgia
8		Midazolam	Less inter individual variation and rapid recovery	Patient with renal mpairment may have longer elimination half life for midazolam and its Metabolites may result in slower recovery. ^[22]
9		Pioglitazone	piaglitazone scares over the ant	piaglitazone has significant reduction of the advanced

			diabetic in decrease or risk	type2 diabetes of higher CV risk ^[31]
10		Enalapril	Increase insulin sensitivity, Thus suitable for obese hypertensive patient	Suitable for obese hypertensive patient but do not have any evidence for increasing insulin sensitivity ^[32]
11	False	Enalapril	Antihypertensive safe in Hypertensive patient with asthma	enalapril causes drug cough that can mimic asthma attack ^[33]
12		Levofloxacin	no cardio toxicity	cardiac arrhythmia due to prolongation of QT interval, angioedema is observed as withdrawal symptom. ^[34]
13		Metoprolol	safe in patient with taken CYP2D6 inhibitor drugs	CYP2D6 inhibitor drugs like quinidine, fluoxetine, are likely to increase metoprolol concentration. ^[35]
14	Debatable	Atorvastatin	highly potent lipid lowering agents	Lipid lowering (LDL-C) is dependent on effect of dose of on the lipid lowering agent. 10 mg of 15atorvastatin is equivalent to 0.4 mg of cerivastatin. ^[36]
15		Azithromycin	Superior gastrointestinal tolerability	Gastrointestinal side effects are the most common adverse effects. ^[23]
16		Lactulose	detoxifies liver	lactulose reduce the absorption of ammonia from gut, thereby preventing the complication of liver disease like hepatic encephalopathy. ^[37]
17		Vitamin B complex	useful for muscle of heart	Formulation of vitamin B complex including B6 and B12 damage the thin layer of endothelium. ^[38]
18		Vitamin B complex	Has lipid lowering effects	Vitamin B complex raises the total cholesterol level and triglycerides. ^[38]

The drug promotional practices carried out by marketing department of the pharmaceutical industry have undergone a drastic change from the early days where the categorical detailed information were delivered to the doctors but now the pharmaceutical company are more focused on the brand to increase their sale.^[24]

The accuracy and validity of the information presented in promotional brochures is important because many physicians rely heavily on such information while making prescribing decision.^[3]

The misleading claims in the promotional material have marked effect on the prescription behavior of the physician and the rational use of medication. The irrational use of the drug can lead to for treatment failures, patients suffering unnecessary adverse effects, increase in antibiotic-resistant cases and the waste of patients' money and national health resources.

CONCLUSION AND RECOMMENDATION

The promotional materials like flash card leave behind card, magazines, general information brochures, leaflets, literatures, drugs status of different companies, and any other available printed materials were collected from the hospital and marketing representatives.

None of promotional material have all the requirements given by WHO and/or DDA's criteria on the ethical promotional guideline on promotion. Although some lack information on generic name, dosage form and scientific literature the promotional drugs contain 100% brand name. The entire promotional efforts must be in quality and quantity in the line with the national requirement and appropriate to support the correct use of the product. In the country like Nepal, the applicability of these criteria can help the health professional and requires the extensive study.

The present study shows that the promotional practice of the medicinal drug is rampant in Nepal. The promotional claims made by the pharmaceutical company are overstated so that they magnify the therapeutic values of drug molecules. These misleading claims have greater impact on the health. Thus the extensive and large scale study should be conducted to measure the misleading claims and impact of these material claims in health of patient.

The effectiveness and usefulness of the promotional material could be studied qualitatively and quantitatively. The project was carried in the limited time period. The more intensive study can be performed in order to obtain detailed data. A well-defined and updated ethical criterion for the marketing of medicinal drugs by pharmaceutical companies for providing the information to the health profession should be followed This study may act as a guideline for any further comprehensive studies similar topics.

Acknowledgement

We are grateful to marketing department of different pharmaceutical company for providing us the promotional materials. We are thankful to administration of Bir Hospital, TUTH (Tribhuvan University Teaching Hospital), Patan Hospital. Nidan Hospital Pvt.Ltd, Sumerucity Hospital Pvt. Ltd. We would like to express our heartily appreciation to supervisors and teachers.

Lastly, I would like to thank everyone who helped me directly and indirectly in this study.

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